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Heart Failure and Cardiomyopathies

METABOLOMIC PROFILING IDENTIFIES BIOMARKERS PREDICTING ADVERSE OUTCOMES IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

Moderated Poster Contributions
Heart Failure and Cardiomyopathies Moderated Poster Theater, Poster Hall B1
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Background: Heart failure with preserved ejection fraction (HFpEF) is a heterogeneous disease with poorly characterized phenotypes. Metabolomic profiling (MP) is a novel technique with the potential to distinguish high risk subtypes of HFpEF.

Methods: Targeted mass-spectrometry based MP of 69 metabolites was performed on plasma from 294 HFpEF cases from the CATHGEN biorepository. HFpEF was defined as an ejection fraction ≥ 50% and NYHA class II-IV within the previous 2 weeks. Principal components analysis (PCA) was used for multidimensional data reduction. Multivariate time-to-event analyses examined associations between factor levels and clinical outcomes.

Results: 8 of 14 PCA-derived factors were associated with mortality. Factor 3 (short-chain dicarboxylacylcarnitines: hazard ratio [HR] 1.35 [95% CI, 1.17-1.54], P<0.0001), factor 1 (medium-chain acylcarnitines: HR 1.28 [CI 1.08 - 1.51], P=0.005) and factor 7 (medium-chain acylcarnitines, HR 1.28 [1.08 - 1.51], P=0.004) were associated with increased risk of adverse events. Factor 14 (C22: HR 0.72 [0.56 - 0.92], P=0.008), factor 8 (urea cycle amino acid: HR 0.72 [0.53 - 0.97], P=0.031) and factor 13 (non-esterified fatty acid: HR 0.77 [0.63 - 0.94], P=0.009) were associated with a decreased risk of adverse events (Table).

Conclusion: Metabolites reporting on fatty acid oxidation and urea cycle energetic pathways independently predict adverse outcomes in patients with HFpEF highlighting potential biomarkers and high risk HFpEF subtypes.

Table. Multivariable associations of metabolite factors with mortality, MI, PCI or CABG

Factor	Components	Mortality HR*	P-value	MI, PCI, CABG or death HR*	P-value
1	Medium-chain acylcarnitines	1.28 (1.08 – 1.51)	0.005	1.21 (1.04 - 1.41)	0.012
2	Long-chain dicarboxylacylcarnitines	1.17 (1.06 – 1.30)	0.002	1.16 (1.05 - 1.28)	0.004
3	Short-chain dicarboxylacylcarnitines	1.34 (1.17 – 1.54)	<0.0001	1.21 (1.06 - 1.39)	0.005
4	Long-chain acylcarnitines	1.01 (0.80 – 1.26)	0.947	0.98 (0.80 - 1.21)	0.878
5	Ketone related	1.17 (0.98 – 1.40)	0.080	1.31 (1.10 - 1.57)	0.003
6	Branched-chain amino acids	0.89 (0.72 – 1.10)	0.279	0.96 (0.78 - 1.17)	0.652
7	Medium-chain acylcarnitines	1.28 (1.08 – 1.51)	0.004	1.15 (0.98 - 1.36)	0.095
8	Urea cycle amino acids	0.72 (0.53 – 0.97)	0.031	0.77 (0.60 - 0.99)	0.045
9	C3 – C5's	1.02 (0.84 – 1.25)	0.817	0.99 (0.82 - 1.20)	0.950
10	Gly, Orn, C5:1	0.93 (0.77 – 1.11)	0.421	0.95 (0.80 - 1.12)	0.540
11	Asx, C5-OH/C3-DC	1.19 (0.99 – 1.42)	0.067	1.11 (0.94 - 1.33)	0.226
12	C18:2-OH	1.34 (1.12 – 1.61)	0.002	1.61 (1.34 - 1.94)	<0.0001
13	NEFA	0.77 (0.63 – 0.94)	0.009	0.81 (0.68 - 0.97)	0.019
14	C22	0.72 (0.56 – 0.92)	0.008	0.71 (0.56 - 0.89)	0.003

Abbreviations: PCA, indicates principal components analysis; HFpEF, Heart Failure with Preserved Ejection Fraction; HFrEF, Heart Failure with Reduced Ejection Fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; HR, hazard ratio; Gly, glycine; Orn, ornithine; Asx, asparagine and aspartic acid; DC, dicarboxylate; OH, hydroxyl; NEFA, non-esterified fatty acid

*Adjusted for age, race, sex, hypertension, diabetes, hyperlipidemia, COPD, BMI, smoking and number of diseased coronary arteries